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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/025,514	12/18/2001	Philip J. Barr	368292000200	6421

25226 7590 10/21/2003

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EXAMINER	
WALICKA, MALGORZATA A	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,514	BARR ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-10 and 12-37* is/are pending in the application.

4a) Of the above claim(s) *3,5-7,9,10,12-15 and 18-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4,8,16 and 17* is/are rejected.

7)☒ Claim(s) *36 and 37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on Sept. 11, 2003 has been entered. Claims 1 and 11 are cancelled; new claims 36 and 37 are added. Claims 2-10 and 12-37 are pending. Claims 3, 5-7, 9-10, 12-15 and 18-35 are withdrawn form consideration as directed to the non-elected invention.

Detailed Office Action

1. Objections

Claims 8 is objected to as depending on claim 3 belonging to the non-elected invention.

Objections to clam 8 made in the previous Office Action, paper No. 12, are withdrawn because Applicants' arguments have been found persuasive.

2. Request for rejoinder

Applicants reiterate their request for rejoinder of method claims 26-35. As indicated in previous Office Actions, the issue will be addressed when allowable composition claims are identified.

3. Rejections

3.1. 35 U.S.C. 112, second paragraph

Rejection maintained

Claims 4, 8, 16 and 17 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for reasons stated on the previous Office Actions, June 6, 2003 and December 3, 2002, and reiterated herein. The phrases "amino acid from about 1 to about 394 of alpha 1 antitrypsin " and "amino acid from about 1 to about 107 of secretory leukocyte protease inhibitor" render the claims indefinite.

The claims are directed to fusion protein comprising amino acid residues acids 1-394 of human AAT and or 1- 107 of SLPI, without giving the sequence identification number. There are known many human AATs, see the rejection for lack of written description bellow, and amino acids 1-394 in one human variant of AAT are not the same as amino acids 1-394 in the other human variant of AAT. Therefore, recitation 1-394 of human AAT and 107 of human SLAPI are indefinite as long as the sequence form, which they originate, is not identified by its sequence identification No. The indefinite recitation renders the claim indefinite.

Rejection withdrawn

Rejection of claims 4, 16, and 17 for the recitation of the term "about" as a relative term is withdrawn, because Applicants' arguments are found persuasive.

3.2. 35 U.S.C. 112, first paragraph

3.2.1. Lack of written description

2, 4, 8 and 16-17 are rejected under 35 U.S.C. 112, first paragraph, for the reason indicated in the previous office Action, paper No. 12 and reiterated herein.

The claims are directed to large and variable genera of fusion proteins.

Claim 2 is directed to a genus of the fusion proteins encompassing proteins comprising:

1) any human alpha 1-antitrypsin or a functionally active portion thereof, and

2) any human secretory leukocytes protease inhibitor or a functionally active portion hereof,

wherein the fusion protein has protease inhibitor activity.

The scope of the claim encompasses a large genus of fusion proteins that comprise an alpha 1-antitrypsin inhibitor and secretory leukocytes protease inhibitor, as well as functionally active fragments thereof, wherein both components of the fusion protein originate form human, and wherein the fusion protein has protease inhibitor activity. The claim does not state what is the structure of the fusion protein, i.e. what is the structure of the components and how they are connected.

Applicants teach only two representatives of the genus wherein the species have the function of both protease inhibitors and structure described by amino acid sequences of SEQ ID NOs: 8 and 16 (SLAPI and reverse SLAPI). This is, however, insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. The description of the invention is insufficient,

because the Applicants' intention is a multifunctional inhibitor, see the title of the disclosure that has activities of both inhibitors, i.e. the activity of AAT and secretory leukocyte protease inhibitor. Any combination of any two inhibitors, or their functional parts, does not necessary lead to a fusion protein having the desired function specificities of both components. The claim does not state how the components of the fusion protein are connected and does not state the structure of the components so that they have the claimed function. One skilled in the art realizes that the change of one amino acid of a protein my lead to its inactivation. Therefore not any combination of any human AAT and SLPI or their functionally active fragments will result in a fusion protein which is intended to be an inhibitor having both inhibitory functions. In addition, a linker joining two components and any additional sequences comprised in the fusion protein are likely to negatively influence the desired function of the fusion protein.

Human AAT of Table 2 has more than 50 natural allelic forms, and the definition of "functionally active portion thereof' encompasses any protein having the AAT function, including man-modified forms. Also SLPI is a generic protein and the genus comprises any variant of human SLPI. Furthermore, it is not clear that the term "human AAT" and "human SLAPI" encompass only variants of a single gene of it. These terms are broad enough to encompass other genes encoding proteins having inhibitory effects on alpha-antitrypsin or secretory leukocyte protease.

In conclusion, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claim 4 is directed to a genus of the fusion proteins encompassing proteins comprising:

1) amino acids from about 1-to about 394 of any human alpha 1-antitrypsin, and

2) amino acids from about 1-about 107 of any human secretory leukocyte protease inhibitor,

wherein the fusion protein has protease inhibitor activity.

The scope of the claim encompasses a large genus of fusion proteins that comprise amino acids from about 1-to about 394 of any human alpha 1-antitrypsin and amino acids from about 1-about 107 of any human secretory leukocytes protease inhibitor wherein the fusion protein has protease inhibitor activity. The claim does not state what is the structure of the fusion protein, i.e. what is the structure of the components and how they are connected, as well what are the other sequences comprised in the fusion protein. Although the claim recites amino acids from about 1-to about 394 of any human alpha 1-antitrypsin and amino acids from about 1-about 107 any human secretory leukocytes protease inhibitor, the claim does not recite the way the both components are connected, neither the claim identifies human alpha 1-antitrypsin and human secretory leukocytes protease inhibitor sequences by their sequence identification number. The currently known number of allelic variants of human alpha 1-antitrypsin is 50. This number, however does not include unknown variants related to human pathologies or any recombinant and man-modified forms. Although human secretory leukocyte protease inhibitor does posses many allelic

variants, the variants created by recombinant production of the protein or modified forms are probable. In addition, amino acids 1-394 and 1-107 can be connected using a great number of linkers and additional amino acid sequences are to be included in the fusion protein.

Applicants teach only two representatives of the genus wherein the species have the function of both protease inhibitors and structure described by amino acid sequences of SEQ ID NOs: 8 and 16 (SLAPI and reverse SLAPI). This is, however, insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. The description of the invention is insufficient, because the Applicants' intention is a multifunctional inhibitor, see the title of the disclosure, that has activities of both inhibitors, i.e. the activity of AAT and secretory leukocyte protease inhibitor. Any combination of amino acids sequences comprising 1-349 and 1-107 of human AAT and SLPI does not necessary lead to a fusion protein having the desired function specificities of both components. The claim does not state how the components of the fusion protein should be connected and does not state the structure of the components so that the fusion protein had the claimed function. One skilled in the art realizes that if two active fragments of proteins are comprised in a fusion protein, the fusion protein may be not active because the amino acid sequence used for connection of both components may inactivate them. In addition, any other components of the fusion protein that are indicated by the language "comprising" may negatively influence the fusion protein function. Thus, not any combination of 1-to about 394 of any human alpha 1-antitrypsin and amino acids from about 1-about 107 of any

human secretory leukocytes protease inhibitor will result in a fusion protein which is an inhibitor having both functions.

In conclusion, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 8 and 16-17 is included to rejection of claim 2 or 4, as dependent claims that do not correct deficiencies of the base claims.

In response to the rejection, on page 13, line 17 of their Remarks Applicants write,

> "The linkage of the protease inhibitors into fusion proteins is also described in detail in the specification, see, e.g., ¶69, including two orientations used in the working examples, as well as possible additional amino acids that may be inserted between the protease inhibitors."

Paragraph 69 of the specification teaches,

"The fusion of the two proteins of the fusion protein may be by means of a simple peptide bond, or there may be one or more additional amino acids which comprise the fusion linkage between the two proteins of the fusion protein. In a preferred embodiment, there is a methionine between the AAT and the SLPI. There may be additional sequences in one or more locations of the fusion proteins of the invention."

Further, on page 13, line 26, Applicants conclude:

"Thus, the claims themselves recite the structure and function of the claimed fusion proteins, and the specification further describes structural and functional characteristics of the claimed proteins in detail. This, in itself, is sufficient to satisfy the written description requirement."

Applicants' argument regarding detailed description of the structure of the fusion protein is found not persuasive for the following reasons. Paragraph 69 to which Applicants refer the examiner's attention uses language "may", therefore, interpreting claims 2, 4 and 8 in the light of the disclosure is vague, because it is unknown what amino acids or pairs of them, as well as what additional sequences and their placement in the fusion protein, are included or excluded form the scope of the invention.

In summary, claims 2, 4, 8 and 16-17 remain rejected under 36 USC section 112, first paragraph as lacking written description of structure, because they do not include any structural limitation at all. Applicants repeatedly argue that claims recite both structure and function, but the fact is they do not. The claims are limited only functionally.

4. Conclusion

No claim is in conditions for allowance, however, as stated in the Office Action of June 3, 2003, the claims contain allowable subject matter. Claims 36 and 37 are objected to as depending on rejected claim 4 but would be allowable if rewritten in an independent form.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m. If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Patent Examiner